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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/775,687 | 02/02/2001 | Noel K. Maclaren | BII-001CP | 3472 |

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| EXAMINER | |
|---|---|
| LUCAS, ZACHARIAH | |
| ART UNIT | PAPER NUMBER |
| 1648 | |

DATE MAILED: 09/10/2002 10

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/775,687 | MACLAREN ET AL. | |
| | Examiner | Art Unit | |
| | Zachariah Lucas | 1648 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *19 August 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-24, and 27-32* is/are pending in the application.

4a) Of the above claim(s) *1-12,19,21,22,24 and 28-32* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13-18,20,23 and 27* is/are rejected.

7)☒ Claim(s) ____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 5+6 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

## DETAILED ACTION

### *Election/Restrictions*

1. Applicant's election with traverse of Group XI in Paper No. 9 is acknowledged. This Group currently consists of claims 13-18, 20, 23, and 27. The traversal is limited to the restriction among Groups IX-XII. Paper 9, page 5. The traversal is on the ground(s) that a claim is present that is generic to all of the identified Groups. This is not found persuasive because the presence of a linking claim does not make a restriction requirement among Groups of inventions within a linking claim improper. Rather, the presence of the linking claim simply means that the claims will be examined under the USPTO linking claim practice. See MPEP §§ 809 and 809.03. As the methods of Groups IX-XII each relate to a method wherein a different product is being used, therefore having different modes of operation, the methods are distinct.

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 1-12, 28, 29, and 30 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 9.

3. Newly amended or submitted claims, and those claims 13-16,18, 22, 31, and 32 either include, or are directed to, inventions that are independent or distinct from the inventions originally claimed. As such, the following new Groups of inventions have been added to the restriction requirement under 35 U.S.C. (s) 121. The new inventions are directed to either

(XVII) methods of preventing the development of an autoimmune disorder by administering a multicellular parasite; or

(XVIII) methods of preventing the development of an autoimmune disorder by administering a LPS from a multicellular parasite.

These methods are unrelated to each other, and to the methods of the other Groups, because they use different products in the methods, and therefore have different modes of operation. Restriction is proper among the Groups because each of the methods will require a different search that is not co-extensive with the searches for the other methods. Accordingly, claim 32 is withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

4. Claims 19, 22, 24, and 31 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 9.

***Information Disclosure Statement***

5. The following reference is in a foreign language accompanied by an English abstract. Due to this, the reference has been examined only to the extent of the disclosure in the abstract.
WO 98/44928.

***Specification***

6. The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction of the following is required: Claim 23 refers to a method of preventing an autoimmune disease by administrating an enhancing agent wherein the agent is a bacterial cell lysate. However, such an enhancing agent is not disclosed in the specification. Appropriate correction is required.

## *Claim Objections*

7. Claim 16 objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 16 is describing a separate method from claim 13 from which it depends, and is therefore not further limiting to that claim.

## *Claim Rejections - 35 USC § 112*

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claim13-18, 20, 23, and 27 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of using some enhancing agents to ameliorate or treat some autoimmune diseases, does not reasonably provide enablement for methods of using any bacterial enhancing agents to prevent any autoimmune disease. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. While the art recognizes that some bacteria and some substances derived therefrom may be used to treat some autoimmune diseases, the applicant has not shown that one skilled in that art may treat or prevent any autoimmune disease by administering to the subject any bacterial cell or substance derived therefrom. Nor has the applicant provided adequate guidance as to what bacterial or parasitic species or strains, or substances, will be effective in the claimed methods. Thus, the claims are

not fully enabled for two reasons: 1) the applicant has not shown that every bacterial cell or substance will be effective in treating autoimmune diseases, and 2) the applicant has not shown that every autoimmune disease is susceptible to treatment by the bacterial compositions.

The first point, that not every bacterial substance will be effective in treating autoimmune diseases, is illustrated by the disclosure of U.S. Patent Number 5,268,170. In column 1 (lines 49-57) of the patent, the specification states that some factions of the same bacterial line was effective in treating adjuvant arthritis (a model for the autoimmune disease rheumatoid arthritis), while another appeared to be causative of the disease. It further indicates that another species of bacteria, Mycobacterium vaccae, appeared to be free of the components that cause the disease altogether. Thus, the reference shows that, until experimentation was done, it would not be obvious to one skilled in the art which bacterial species would provide effective and safe therapeutics against any particular disease, even in a genus where operative species were already known. As the applicants have not provided any guidance in the specification that would lead those in the art to such bacterial species and components, the applicants have not provided a sufficient disclosure to enable the full extent of the claimed inventions.

The second basis for the lack of enablement rejection is that the applicant has provided no disclosure that would support the claim that any autoimmune disease may be treated or prevented with any bacterial strain, or even any of those 6 strains that are named in the claims. While the art does indicate that some species of the some strains may be effective in treating some forms of autoimmune diseases, there is no general recognition that bacterial lysates or other compositions will be effective against any autoimmune disease. For example, although Mycobacteria were known to be effective against rheumatoid arthritis in 1985 (see PCT

document WO 85/05034), those in the art in 1998 were not willing to say that the bacterial could be used to treat every autoimmune disease alone, although it could be used as an effective adjuvant and carrier for other antigenic particles to treat other forms of autoimmune diseases. See e.g., U.S. Patent Number 5,830,475, col. 1, lines 33-40, and col. 2, lines 41-48. Due the lack of this expectation of bacterial compositions in the art, and because the specification has neither shown that bacterial compositions are inherently effective in treating autoimmune diseases, or provided guidance to those in the art that would lead towards compositions that would be effective, the applicant has not enabled the claims to the full extent of the claimed inventions.

***Claim Rejections - 35 USC § 102***

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

11. Claims 13-18, 20, and 23 are rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent Number 5,830,475, issued to Aldovini et al. (Aldovini) and by published PCT application WO 85/05034, naming Stanford et al. as inventors. The rejected claims describe methods of preventing or ameliorating autoimmune diseases by administering to a subject an enhancing agent wherein the agent is a bacterium or a substance derived therefrom.

The two references disclose that Mycobacteria and fractions therefrom may be used to treat or vaccinate against autoimmune arthritic diseases. See, Aldovini, col. 2, lines 41-48; and Stanford, abstract. The references teach that rheumatoid arthritis is a form of autoimmune disease. Aldovini, id.; Stanford p. 1, lines 1-4. Aldovini teaches that whole recombinant mycobacterial cells may used as live recombinant vaccine vesicles (col. 1, lines 33-40), while Stanford teaches that the bacteria, and solutions of the fractionated bacteria (therefore lysates) may be used in treatments and vaccines (p. 2, lines 18-22). As the references teach that the bacterial solutions may be used both as a vaccine, and for curative purposes, they inherently teach that the solutions may be administered to both subjects known to be at risk for an autoimmune disorder (curative), and those not known to be at risk (vaccine). Stanford further teaches that the compositions of the mycobacteria may be administered orally. Stanford, claim 7.

12. Claims 13, 14, 16, 20, 21, and 27 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent Number 6,350,457, issued to Watson et al. (Watson). The claims are described above, except for claim 27, which limits the methods to the treatment of one of the following autoimmune diseases: asthma, allergic rhinitis, and hay fever. The claims are rejected based on Watson, which teaches that derivatives of Mycobacteria vaccae cells may be administered to a subject to prevent and treat these diseases. Abstract; col. 4, lines 45-51 (allergic rhinitis includes

hay fever); and col. 6, lines 44-49. Among the derivatives that may be used are mycobacterial cells subjected to alkaline or acidic hydrolysis. Thus, the patent teaches the use of agents derived from mycobacterium to treat asthma, hay fever, and allergic rhinitis. The patent further teaches that the composition may be administered through the nose or mouth, thus orally. Col. 7, lines 27-30.

13. Claims 13, 14, 16, 17, 20, and 23 are rejected under 35 U.S.C. 102(b) as being anticipated by Qin et al., J. Immunology 150:2072-2080 (Qin). These claims describe methods of preventing or treating autoimmune diseases by administering to a subject a bacterium or bacterial lysate. The reference discloses that the administration of Complete Freunds Adjuvant helps to prevent and to delay onset of (ameliorate) an autoimmune disease – insulin-dependent diabetes mellitus. Abstract. As the adjuvant contains a mycobacterial cell wall, and as the application contains no definition for a bacterial lysate that is contradictory to the inclusion of the adjuvant in the definition, the reference contains a bacterial lysate. The reference therefore anticipates the stated claims.

14. Claims 13-18, 20, and 27 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent number 6,361776 issued to Alain Delcayre (Delcayre). The claims are described above. Delcayre describes the use of polypeptides and polynucleotides derived from Mycobacteria to treat diseases, including asthma and allergic rhinitis. Col. 3, lines 5-10, 28-30, 34-37, and 43-46. The patent teaches that the vaccines compositions may be formulated for oral administration. Col. 10-11. Because the patent teaches the use of, and methods using, proteins

derived from Mycobacteria to treat asthma and allergic rhinitis, and the claims rejected read on substances derived from Mycobacteria, the claims are anticipated by the reference.

***Claim Rejections - 35 USC § 103***

15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

16. Claims 13-18, 20, 23, and 27 rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent Number 6,433,013 issued to Verschoor et al. (Verschoor), in view of Aldovini; and further in view of Watson and Qin. The claims are described above. Verschoor teaches that certain cell membrane molecules from mycobacterial cell membranes may be used to treat autoimmune disorders, including allergies. Further, the reference teaches that the cell membrane lipids may be administered with a bacterial protein derived from a Mycobacterium. Col. 2, lines 18-27. Because Aldovini teaches that Mycobacterium are highly effective adjuvants (col. 1, lines 33-40), and because Verschoor suggests the use of the bacterium as adjuvants it would have been obvious to one of ordinary skill in the art to use these compositions together to treat autoimmune allergies. However, the teachings do not teach the use of bacterial lysates.

The teachings of Watson and Qin are described above. Watson taught that derivatives of mycobacterium could be used to treat hay fever, asthma, and allergic rhinitis. Qin taught that administration of Complete Freunds Adjuvant (which contains mycobacterial cell wall

fragments) helps to prevent and to delay onset of (ameliorate) an autoimmune. Abstract. Watson teaches that mycobacterial cell adjuvants are effective in treating hay fever, asthma, and allergic rhinitis. Qin teaches that adjuvants comprising cell wall fragments (bacterial lysates) of these bacteria are likewise effective adjuvants. It would therefore have been obvious to one of ordinary skill in the art to use the cell components as the adjuvant in the method of Verschoor. One of ordinary skill in the art would have had a reasonable expectation of success in the combination as all of the elements combined were known to be effective in the treatment, and no reason existed to indicate that combining the elements together would yield less effective results.

***Conclusion***

17. The following prior art reference is made of record and is considered pertinent to applicant's disclosure. However, while relevant they are also not used as a basis for rejection for the stated reasons.

> U.S. Patent Number 5,268,170, issued to Van Eden et al. this reference teaches that it was known in the art that mycobacteria and mycobacterial fractions might be used to treat and vaccinate against autoimmune arthritis. The reference is considered redundant to the Stanford document above.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 703-308-4240. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 703-308-4027. The fax phone numbers for the

organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

L. Lucas
Patent Examiner
September 9, 2002

JAMES HOUSEL
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600